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(71) Applicant ( <i>for all designated States except US</i> ): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
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(74) Agents: WALES, Michele, M. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).			
(54) Title: HUMAN PANCREAS AND PANCREATIC CANCER ASSOCIATED GENE SEQUENCES AND POLYPEPTIDES			
(57) Abstract			
<p>This invention relates to newly identified pancreas or pancreatic cancer related polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "pancreatic cancer antigens", and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such pancreatic cancer antigens for detection, prevention and treatment of disorders of the pancreas, particularly the presence of pancreatic cancer. This invention relates to the pancreatic cancer antigens as well as vectors, host cells, antibodies directed to pancreatic cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing disorders related to the pancreas, including pancreatic cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of pancreatic cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.</p>			

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340                    345                    350

Tyr Glu Glu Asn Gly Thr Asp Leu Ser Gly Ala Gly Asp Pro Tyr Leu  
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<223> Xaa equals any of the naturally occurring L-amino acids

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20                    25                    30

Met Ala Lys Leu Arg Gln Lys Asn Pro Arg Ala Val Arg Gln Ala Glu  
35                    40                    45

Glu Val Arg Gly Leu Glu His Leu His Met Asp Val Ala Val Asn Phe  
50                    55                    60

Ser Gln Gly Ala Leu Leu Ser Pro His Leu His Asn Val Cys Ala Glu  
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Pro Cys Val Cys His Tyr Gly Leu Ser Leu Ala Trp Tyr Pro Cys Met  
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Leu Lys Tyr Cys His Ser Arg Asp Arg Pro Thr Pro Tyr Lys Cys Gly  
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*What Is Claimed Is:*

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
  - (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
  - (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;
  - (g) a polynucleotide which is a variant of SEQ ID NO:X;
  - (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
  - (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
  - (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide

10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least  
5 95% identical to a sequence selected from the group consisting of:
  - (a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;
  - 10 (c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - 15 (e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (f) a variant of SEQ ID NO:Y;
  - (g) an allelic variant of SEQ ID NO:Y; or
  - (h) a species homologue of the SEQ ID NO:Y.
- 20 12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
- 25 13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
- 30 15. A method of making an isolated polypeptide comprising:

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
22. A method of identifying an activity in a biological assay, wherein the method comprises:
  - 5 (a) expressing SEQ ID NO:X in a cell;
  - (b) isolating the supernatant;
  - (c) detecting an activity in a biological assay; and
  - (d) identifying the protein in the supernatant having the activity.
- 10 23. The product produced by the method of claim 20.

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7 C12N15/11 C12N15/12 C12N15/62 C12N15/86 C12N5/10 C07K14/47 C07K16/18 A61K31/713 C12Q1/68 G01N33/577 G06F17/30					
According to International Patent Classification (IPC) or to both national classification and IPC					
B. FIELDS SEARCHED					
Minimum documentation searched (classification system followed by classification symbols)					
IPC 7 C12N C07K A61K C12Q G01N G06F					
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched					
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)					
EPO-Internal, BIOSIS, MEDLINE, WPI Data					
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.
X	DATABASE EMBL [Online] 26 December 1999 (1999-12-26) BIRREN B. ET AL: "Homo sapiens chromosome 11, clone RP11-707D17" Database accession no. AC18997 XP002170377 nts. 20-1487 ---				2-4, 15-17, 21-26
P,X	WO 00 55320 A (HUMAN GENOME SCIENCES INC ; ROSEN CRAIG A (US); RUBEN STEVEN M (US)) 21 September 2000 (2000-09-21) SEQ ID NOS.171 and 630 page 494; claim 19 ---				2-4, 15-27, 29-33
A	WO 93 16180 A (MAX PLANCK GESELLSCHAFT ; UNI DEGLI STUDI G D ANNUNZIO C (IT)) 19 August 1993 (1993-08-19) ---				-/-
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.			<input checked="" type="checkbox"/> Patent family members are listed in annex.		
° Special categories of cited documents :					
'A' document defining the general state of the art which is not considered to be of particular relevance			'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention		
'E' earlier document but published on or after the international filing date			'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone		
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'P' document published prior to the international filing date but later than the priority date claimed					
Date of the actual completion of the international search			Date of mailing of the international search report		
28 June 2001					
Name and mailing address of the ISA			Authorized officer		
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl Fax: (+31-70) 340-3016			Blanco Urgoiti, B		

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ANISOWICZ A ET AL: "A NOVEL PROTEASE HOMOLOG DIFFERENTIALLY EXPRESSED IN BREAST AND OVARIAN CANCER" MOLECULAR MEDICINE, US, BLACKWELL SCIENCE, CAMBRIDGE, MA, vol. 2, no. 5, 1 September 1996 (1996-09-01), pages 624-636, XP002060076 ISSN: 1076-1551</p> <p>---</p> <p>BERGSTROM DAVID E ET AL: "Regulatory Autonomy and Molecular Characterization of the Drosophila cut at first Gene." GENETICS, vol. 139, no. 3, 1995, pages 1331-1346, XP001009906 ISSN: 0016-6731 cited in the application</p>	

## Information on patent family members

International Application No

PCT/US 01/00899

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 0055320	A 21-09-2000	AU 3395900	A	04-10-2000
		AU 3617600	A	04-10-2000
		AU 3617700	A	04-10-2000
		AU 3619400	A	04-10-2000
		AU 3619500	A	04-10-2000
		AU 3869400	A	04-10-2000
		WO 0055173	A	21-09-2000
		WO 0055350	A	21-09-2000
		WO 0055351	A	21-09-2000
		WO 0055180	A	21-09-2000
		WO 0055174	A	21-09-2000
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WO 9316180	A 19-08-1993	IT 1254309	B	14-09-1995
		AU 3497893	A	03-09-1993
		CN 1076489	A	22-09-1993
		ZA 9301101	A	17-08-1994
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